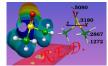**About using Ante_R.E.D., R.E.D. & X_R.E.D.**

http://q4md-forcefieldtools.org/RED/

For more information:
See Tutorials @ http://q4md-forcefieldtools.org/Tutorial/
R.E.DD.B. http://q4md-forcefieldtools.org/REDDB/
R.E.D. Server http://q4md-forcefieldtools.org/REDS/

The examples presented in this distribution are slightly different to these available in the R.E.D.-III.2 tools version.
Most of these examples presented are available in R.E.DD.B. as well.

Last update of this document: October 1ˢᵗ, 2009

-1- Executing Ante_RED-1.3

To execute Ante_R.E.D., use "perl" as it follows:

```
perl Ante_RED-1.3.pl PDB-file
    or
perl Ante_RED-1.3.pl PDB-file > Ante_RED.log &          PDB-file = Your PDB file
```

- Create a csh script for multiple Ante_RED executions:

```
#!/bin/csh
#
touch Ante_RED.log
foreach PDBFILE (*.pdb)
  perl Ante_RED-1.3.pl $PDBFILE >> Ante_RED.log
end
```

- Remark: The PDB-file(s) & Ante_RED-1.3.pl have to be in your working directory.

* Example-1
Using the DMSO.pdb file (available in the directory `HowTo/2-Dimethylsulfoxide`) provided in the R.E.D.-III.3 tools distribution, execute:

```
cp Ante_RED-1.3.pl HowTo/2-Dimethylsulfoxide
cd HowTo/2-Dimethylsulfoxide
perl Ante_RED-1.3.pl DMSO.pdb > Ante_RED.log
```

Then, compare the DMSO-out.p2n file generated using Ante_R.E.D. with the Mol_red1.p2n file (available in the directory `HowTo/2-Dimethylsulfoxide`). Mol_red1.p2n file is an example of input file to be used with R.E.D.-III.3.

* Example-2
Using the EtOH*$i*.pdb files (conformations: *$i*=2; available in the directory `HowTo/1-Ethanol`) provided in the R.E.D.-III.3 tools distribution, execute:

```
cp Ante_RED-1.3.pl HowTo/1-Ethanol
cp Scripts/0Multi-Ante-RED.csh HowTo/1-Ethanol
cd HowTo/1-Ethanol
csh 0Multi-Ante-RED.csh
```

Then, compare the EtOH*$i*-out.p2n files generated using Ante_R.E.D. with the Mol_red1.p2n file. Mol_red1.p2n is an example of input file for R.E.D.-III.3 (charge derivation & force field library building involving two conformations).

-2- Using RED-vIII.3

To execute R.E.D. & modify R.E.D. variables, see the "MAIN PROGRAM" section in the source code: *i.e.* `Lines 3843-3870`.

These options are summarized below:

```
$XRED = "Off";                  # If XRED="ON", R.E.D. is executed using the X R.E.D. graphical interface (see below).

$NP = "1";                      # Number of cpu(s)/core(s) used in parallel in QM calculations; used only if XRED="OFF".

$QMSOFT = "PC-GAMESS";          # "GAMESS-US" (GAMESS-US or WinGAMESS), "PC-GAMESS", or
                                # "GAUSSIAN" (g09, g03, g98 or g94, the latest version found is used) is interfaced in QM calculations;
                                # used only if XRED="OFF".

$DIR = "Data-RED";              # Directory name where data generated by R.E.D. are stored; useful only if XRED="OFF".
                                # If $DIR = "", $DIR is automatically set to "Data-RED".
                                # When using $Re_Fit = "On" do not change $DIR between the first R.E.D. job & the re-fit job(s).

$OPT_Calc = "Off";             # Geometry optimization is carried out only if $OPT_Calc = "ON"; used only if XRED="OFF".

$MEPCHR_Calc = "On";           # MEP computation & charge fitting are carried out if $MEPCHR_Calc = "ON";
                                # used only if XRED="OFF".

$Re_Fit  = "Off";              # Charges are re-fitted & force field (FF) library(ies) re-built from a previous R.E.D. job;
                                # used only if XRED="OFF".
                                # If $Re_Fit = "On", $OPT_Calc & $MEPCHR_Calc are automatically set to "Off"

$CHR_TYP = "RESP-A1";          # Charge models available:
                                # "RESP-A1, RESP-A2, RESP-C1, RESP-C2, ESP-A1, ESP-A2, ESP-C1, ESP-C2";
                                # -1- RESP-A1: HF/6-31G* Connolly surface algo., 2 stage RESP fit qwt=.0005/.001
```
 # Used in the Cornell et al., Kollman et al., Cheatham et al., Wang et al. & Hornak et al. AMBER force fields.

=> You could execute the "Corn2Duan.csh" script to modify RED-III.3 so that the RESP-A1 charge model can be used to handle the charge model developed by Duan et al. [i.e. B3LYP/cc-pVTZ SCRF(IEFPCM,Solvent=Ether)//HF/6-31G] when using the Gaussian 2003 program or the charge model developed by Cornell et al.**

```
                                # -2- RESP-A2: HF/6-31G* Connolly surface algo., 1 stage RESP fit qwt=.01
```
 # Created by analogy to the RESP-C2 charge model.
```
                                # -3- RESP-C1: HF/6-31G* CHELPG algo., 2 stage RESP fit qwt=.0005/.001
```
 # Created by analogy to the RESP-A1 charge model.
```
                                # -4- RESP-C2: HF/6-31G* CHELPG algo., 1 stage RESP fit qwt=.01
```
 # Used in the GLYCAM force fields.
```
                                # -5- ESP-A1: HF/6-31G* Connolly surface algo., 1 stage RESP fit qwt=.0000
```
 # Used in some AMBER, OPLS & CHARMM force field based simulations.
```
                                # -6- ESP-A2: HF/STO-3G Connolly surface algo., 1 stage RESP fit qwt=.0000
```
 # Used in the old Weiner et al. AMBER force field.
```
                                # -7- ESP-C1: HF/6-31G* CHELPG algo., 1 stage RESP fit qwt=.0000
```
 # Used in some OPLS & CHARMM force field based simulations
```
                                # -8- ESP-C2: HF/STO-3G CHELPG algo., 1 stage RESP fit qwt=.0000
```
 # Created by analogy to the ESP-A2 charge model.
```
                                # -9- DEBUG: Do not use the DEBUG mode for generating correct charge values !!!
                                #    The DEBUG mode could be used to (I) quickly get an idea of "what is done", (ii) debug the source code
                                #       & (iii) create new functionalities.
                                # useful only if XRED="OFF".
```

To execute R.E.D., use "perl" as it follows:

```
perl RED-vIII.3.pl
    or
perl RED-vIII.3.pl > RED-vIII.log &
    or
time perl RED-vIII.3.pl   (to get the time required for this command)
```

R.E.D. can now be executed in three modes:

- Mode 1

```
$OPT_Calc    = "On";
$MEPCHR_Calc = "On";
$Re_Fit      = "Off";
```

In this mode the geometry optimization, MEP computation and charge fitting steps are handled by the R.E.D. program.

The "Mode 1" only requires the P2N-file(s) & RED-vIII.3.pl to be in your working directory. The file name(s) of the P2N-file(s) has(have) to be "Mol_red$n.p2n" ("$n" is the number of molecule(s) involved in charge derivation and force field library building). Althought "Mode 1" seems simpler to "Mode 2", <u>such an approach is not recommended</u> when deriving RESP or ESP charge values involving multiple-molecules and multiple-conformations. This is because it is unlikely that all the geometry optimization jobs for the different molecules and conformations converge. In the latter case, this leads to a failed R.E.D. execution (see the R.E.D. tools tutorial for more information @ http://q4md-forcefieldtools.org/Tutorial/).

* Example-1
Using the Mol_red1.p2n file (directory HowTo/1-Ethanol) provided in this R.E.D.-III.3 tools distribution, execute:

```
cp RED-vIII.3.pl HowTo/1-Ethanol
cd HowTo/1-Ethanol
perl RED-vIII.3.pl > RED-vIII.log &
```

RESP charge derivation involving two conformations of a single molecule (as defined in the Cornell *et al.* force field) and force field library building are carried out by R.E.D.

See the corresponding "W-10" R.E.DD.B. project @ http://q4md-forcefieldtools.com/REDDB/Projects/W-10/ as well.

- Mode 2

```
$OPT_Calc    = "Off";
$MEPCHR_Calc = "On";
$Re_Fit      = "Off";
```

In this mode only the MEP computation and charge fitting steps are handled by the R.E.D. program.

The "Mode 2" requires the P2N-file(s), QM geometry optimization output file(s) & RED-vIII.3.pl to be in your working directory. The file name(s) of the P2N-file(s) has(have) to be "Mol_red$n.p2n" ("$n" is the number of molecule(s) involved in charge derivation and force field library building). The names of the corresponding QM geometry optimization outputs have to be "Mol_red$n.log".

Let's use the default RESP-A1 charge model in all the examples below.
Modify the $QMSOFT & $NP variables in the R.E.D. source code according to your choice as well.

* Example-2
Using the Mol_red1.p2n & Mol_red1.log files (directory HowTo/2-Dimethylsulfoxide) provided in the R.E.D.-III.3 tools distribution, execute:

```
cp RED-vIII.3.pl HowTo/2-Dimethylsulfoxide
cd HowTo/2-Dimethylsulfoxide
perl RED-vIII.3.pl > RED-vIII.log &
```

RESP charge derivation (as defined in the Cornell *et al.* force field) involving a single molecule and force field library building in the Tripos mol2 file format are carried out by R.E.D. The force field library you are looking for is "Mol_m1-o1.mol2". See the corresponding "W-4" R.E.DD.B. project @ http://q4md-forcefieldtools.org/REDDB/Projects/W-4/.

Example-3

Using the `Mol_red$n`.p2n & `Mol_red$n`.log files (*$n* = 3; directory `HowTo/3-Solvents`) provided in the R.E.D.-III.3 tools distribution, execute:

```
cp RED-vIII.3.pl HowTo/3-Solvents
cd HowTo/3-Solvents
perl RED-vIII.3.pl > RED-vIII.log &
```

RESP charge derivation involving three molecules and force field library building are carried out by R.E.D. See the corresponding "W-46" R.E.DD.B. project @ http://q4md-forcefieldtools.org/REDDB/Projects/W-46/.

Execute "`xleap -f LEaP-script.cmd`" to load these three force field libraries in LEaP.

Example-4

Using the `Mol_red1`.p2n & `Mol_red1`.log files (directory `HowTo/4-Fragment-1`) provided in the R.E.D.-III.3 tools distribution, execute:

```
cp RED-vIII.3.pl HowTo/4-Fragment-1
cd HowTo/4-Fragment-1
perl RED-vIII.3.pl > RED-vIII.log &
```

RESP charge derivation involving a single molecule (as defined in the Cornell *et al.* force field) and force field library building for the central fragment of the alpha-aminoisobutyric acid are carried out by R.E.D. The force field library you are looking for is "`Mol_m1-o1-sm.mol2`".

Execute "`xleap -f LEaP-script-4-F.cmd`" to load this force field library in LeaP.

See the corresponding "F-3" R.E.DD.B. project @ http://q4md-forcefieldtools.com/REDDB/Projects/F-3/.

Example-5

Using the `Mol_red$n`.p2n & `Mol_red$n`.log files (*$n* = 2; directory `HowTo/5-Fragment-2`) provided in the R.E.D.-III.3 tools distribution, execute:

```
cp RED-vIII.3.pl HowTo/5-Fragment-2
cd HowTo/5-Fragment-2
perl RED-vIII.3.pl > RED-vIII.log &
```

RESP charge derivation involving two molecules and force field library building for the $(+)NH_3$-terminal fragment of the alpha-aminoisobutyric acid are carried out by R.E.D. The force field library you are looking for is "`Mol_MM/Mol_m2-o1-mm1.mol2`".

Before claiming there is a bug, please, read http://q4md-forcefieldtools.org/Tutorial/Tutorial-1.php#19
& http://q4md-forcefieldtools.org/Tutorial/leap.php.

Execute "`xleap -f LEaP-script-5-F.cmd`" to correct the Cartesian coordinates & load this force field library in LEaP.

See the corresponding "F-7" R.E.DD.B. project @ http://q4md-forcefieldtools.com/REDDB/Projects/F-7/.

Example-6

Using the `Mol_red$n`.p2n & `Mol_red$n`.log files (*$n* = 2; directory `HowTo/6-Fragment-3`) provided in the R.E.D.-III.3 tools distribution, execute:

```
cp RED-vIII.2.pl HowTo/6-Fragment-3
cd HowTo/6-Fragment-3
perl RED-vIII.3.pl > RED-vIII.log &
```

RESP charge derivation involving two molecules and force field library building for the central fragment of the deoxyadenosine nucleotide are carried out by R.E.D. The force field library you are looking for is "`Mol_MM/Mol_m2-o1-mm1.mol2`".

Before claiming there is a bug, please, read http://q4md-forcefieldtools.org/Tutorial/Tutorial-1.php#19
& http://q4md-forcefieldtools.org/Tutorial/leap.php.

Execute "`xleap -f LEaP-script-6-F.cmd`" to correct the Cartesian coordinates & load the force field library in LEaP.

This example is not available in R.E.DD.B. but this fragment belongs to several R.E.DD.B. projects ("F-45" & "F-60" for instance) with a different set of atom charges (as the charge derivation procedure used is different).

- Mode 3 (re-fitting & force field library re-building mode)

```
$Re_Fit     = "On";
```

If `$Re_Fit = "On"`, `$OPT_Calc` & `$MEPCHR_Calc` are automatically set to "`Off`".

A previous R.E.D. job has to be available in your working directory to be able to execute this Mode 3.

* Example-7
First execute the "Example-3" (`$CHR_TYP = "RESP-A1`" is set - run R.E.D. using its Mode 2).
Then, set `$CHR_TYP = "ESP-A1`" & `$Re_Fit = "On`" in RED-vIII.3.pl & re-execute R.E.D. using:

```
perl RED-vIII.3.pl > RED-vIII.log2 &
```

MEP files generated in the first R.E.D. job available in the "Data-RED" directory are used in the re-fitting job.
The directory corresponding to the first R.E.D. job is renamed into "Data-RED-1"
The data corresponding to the Re_Fit job are available in a new "Data-RED" directory.

See the corresponding "W-48" R.E.DD.B. project @ http://q4md-forcefieldtools.com/REDDB/Projects/W-48/.

* Example-8
First execute the "Example-4" (`$CHR_TYP = "RESP-A1`" is set - run R.E.D. using its Mode 2).
Then, set `$CHR_TYP = "ESP-A1`" & `$Re_Fit = "On`" in RED-vIII.3.pl.
Remove (or desactivate) the `INTRA-MCC` keywords with the "`K`" flag in the `Mol_red1.p2n` file & re-execute R.E.D. using:

```
perl RED-vIII.3.pl > RED-vIII.log2 &
```

See the corresponding "F-5" R.E.DD.B. project @ http://q4md-forcefieldtools.com/REDDB/Projects/F-5/.

This re-fitting mode present several other applications. It allows:
-1 ESP-A1 (or RESP-A2) charge fitting after a previous RESP-A1 job (see above), or
-2 modifying atom names and/or adding/removing INTRA-MCC, INTER-MCC and/or INTER-MEQ keywords in P2N files before re-running the fitting step & FF library building, or
-3 correcting errors in the P2N files after a first R.E.D. run and re-running the fitting step & FF library building, or
-4 re-generating the charge fitting step after finding and correcting a bug the R.E.D. source code.
The common point in these five examples is that MEP files used in a first R.E.D. job & these in the re-run job(s) have to be identical!

Thus, Mode 3 does neither allow "RESP-C2" charge fitting after a previous "RESP-A1" run (required MEP files are different *i. e.* based on the CHELPG & Connolly surface algorithms) nor changing the number of molecules, conformations or orientations after a first R.E.D. run (the number of MEP files is different). In these two cases, a full R.E.D job should be re-run (*i. e.* using the Modes 1 or 2).

Warning: R.E.D. does not check MEP files when using the "Re_Fit" mode!

-4- Executing XRED-III.3

Modify the "XRED" variable in RED-vIII.3.pl:
Set XRED="ON" (instead of XRED="OFF", which is the default).

To execute X R.E.D., use "wish" as it follows:

```
wish XRED-III.3.tcl &
```

You can executes R.E.D. in its three different modes and affect the R.E.D. variables previously described without modifying the R.E.D. source code.

-5- Benchmark & checking procedure

Desactivate the XRED variable (if activated), define the QM program you wish to interface as well as the number of cores/cpus to be used in the QM computations in RED-vIII.3.pl. Then, run the "check.csh" csh shell script as it follows:

```
csh check.csh            or
time csh check.csh       (to get the time required for this command)
```

This script needs the data available in the "HowTo" directory and the R.E.D. program belonging to the R.E.D.-III.3 tools distribution. It automatically (i) executes R.E.D. on your machine and (ii) compares the force field libraries derived on your machine to these we have generated using Gaussian 2003 E.01 (available in HowTo/FFLib).

The maximum charge difference observed for an atom charge should not be above 0.0003 e independently of the QM program used. To slightly improve the differences set qtol = 0.1d-5 in resp.f & recompile...

This "check.csh" job took around:
- 5 min. using Gaussian 2009 A.02 & 8 cores Xeon E5430 @ 2.66GHz (Linux CentOS 5.2).
- 10 min. using GAMESS-US Jan 09 (R1) & 8 cores Xeon E5430 @ 2.66GHz (Linux CentOS 5.2).
- 12 min. using Gaussian 2003 E.01 & 4 cores Core 2 Quad Q6600 @ 2.40GHz (Linux CentOS 5.3).
- 14 min. using PC-GAMESS 7.1.F & 4 cores Xeon X5365 @ 3.00GHz (Leopard/Darwin).
- 17 min. using PC-GAMESS 7.1.F & 4 cores Core 2 Quad Q8200 @ 2.33GHz (Vista 64-bit SP1/Cygwin).
- 30 min. using PC-GAMESS 7.1.F & 2 cores Core 2 Duo P8600 @ 2.40GHz (Windows 7/Cygwin).
- 70 min. using WinGamess Jan 09 (R3) & 1 core Core 2 Duo P8600 @ 2.40GHz (Windows 7/Cygwin).

Do you need a new feature which is not yet implemented in R.E.D.-III.3 ?
Develop your own R.E.D. version in agreement with its license agreement.
and/or contact the q4md force field tools team at
contact@q4md-forcefieldtools.org
Regularly look at the bug fixes at the R.E.D. home page.

Need to perform more complex charge derivation and/or force field library building ?
See R.E.D. Server @ http://q4md-forcefieldtools.org/REDS/ to be able to interface R.E.D.-IV.

Please, submit your force field library(ies) in R.E.DD.B. at http://q4md-forcefieldtools.org/REDDB/
to freely share your results with the scientific community.

Need help about the q4md force field tools ?
Please, ask your queries to the *q4md-forcefieldtools* mailing list @ http://lists.q4md-forcefieldtools.org/

We hope you will find the R.E.D.-III.3 tools useful...

The q4md force field tools team